Danish Ministry
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Survey and health assessment (sensitisation only) of chromium in leather shoes

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Contents

Summary and conclusions

In order to obtain softness, durability and flexibility, leather needs to be tanned. Tanning with chromium is by far the most important method of tanning within the leather industry and is used in more than 80% of the leather industry world-wide. However, several studies have indicated that leather products can release chromium as Cr(VI) and Cr(III) compounds which may cause allergic reactions and severe foot eczema.

In a recent study, the development of chromium allergy among patients with eczema was investigated from 1985 to 2007 in the Greater Copenhagen Area in Denmark. A retrospective analysis of contact allergy to chromium in 16,228 patients was made. The frequency of chromium allergy decreased significantly from 3.6% in 1985 to 1% in 1995, but again increased significantly to 3.3% in 2007. The majority of cases were caused by leather products, particularly shoes. German studies support this tendency.

Thus, the main purpose of this study has been to clarify whether Cr(VI) and Cr(III) compounds are released from leather shoes in Denmark in an amount that constitutes a risk of causing allergic reactions.

To clarify this, the following activities have been performed:

- Market survey of volumes of leather shoes available on the Danish market in 2008.
- Purchase of 60 pairs of leather shoes in the Copenhagen area (20 ladies' shoes, 20 men's shoes and 20 children's shoes).
- XRF screening of the 60 pairs of leather shoes. This was to ascertain the amount of chromium present and thereby potentially create a selection criterion for choosing shoes to undergo further migration analysis.
- Migration analysis according to ISO 17075 (an internationally recognised standard for determining Cr(VI) in solutions leached from leather) of 18 pairs of leather shoes.
- Health and risk assessment for allergy using the 18 pairs of leather shoes.

The XRF screening of the 60 pairs of shoes revealed that the typical range of chromium content in leather shoes seems to be between 1 and 3%. The results indicated no correlation between content of chromium and shoe category (ladies', men's or children's shoes) or shoe type (sandals, boots or ordinary shoes). Thus, 18 pairs were selected that represented proportionally all shoe categories (ladies', men's and children's), shoe types (sandals, boots and ordinary shoes), price ranges and amount of chromium (in the upper leather), since the upper leather typically constitutes the major part of skin contact and since there seems to be a slight tendency to allergic reactions occurring on the upper foot. Furthermore, the skin on the upper foot is thinner than the skin on the sole of the foot, thus it may be more susceptible to developing allergic reactions.

Low levels of Cr(VI) may cause allergic contact dermatitis. Patients with Cr(VI) allergy may react to a single occluded exposure to 1 ppm - 3 ppm Cr(VI). The ISO 17075 is the international standard method for detecting and quantifying leachable Cr(VI). The results are a measure of total potential Cr(VI) exposure. The method has a determination limit of 3 ppm (mg/kg), and has been used in this project to identify shoes which pose a risk of Cr(VI) allergy. It was not possible to define a limit value for Cr(III), due to the small number of studies with diverse results.

From the quantitative analysis using ISO 17075 it was found that 8 pairs of shoes of the 18 analysed (corresponding to 44%) had a Cr(VI) release higher than the determination limit of 3 mg/kg (ppm). The median was 6 ppm and the range from 3 to 62 ppm. A sixth of the shoes released more than 10 ppm Cr(VI). Sandals seemed to be over-represented among the shoes with detectable Cr(VI). This is of concern as sandals are more likely to be worn with bare feet and thus the direct exposure to Cr(VI) is likely to be higher. The shoe with one of the highest levels of Cr(VI) release was a children's sandal. No relation was found between Cr(VI) and Cr(III) levels.

The risk when using shoes that release chromium will be influenced in a manner as yet unknown by use conditions, such as moisture, pH, micro-biological contamination and pre-existing skin diseases. This means that shoes with a low level of Cr(VI) may under certain conditions also pose a risk of chromium allergy. However, in general, the higher the dose of allergen, the higher is the risk of allergy.

Persons who have already developed Cr(VI) allergy may be so sensitive that they may even react to levels of Cr(VI) below the determination level.

In three pairs of shoes, low levels of both Cr(VI) and Cr(III) were seen, which indicates that it is technically possible to produce tanned leather without high levels of chromium and consequently a reduced risk of chromium allergy.

1 Background and purpose

1.1 Background

Leather needs to be tanned in order to obtain softness, durability and flexibility that make the leather usable. Tanning with chromium is by far the most important method of tanning within the leather industry and is used in more than 80% of the leather industry world-wide. The chemical used in the tanning process is alkaline chromium(III)sulphate. This chemical reacts with the leather and stabilizes certain proteins, which makes the leather more resistant towards degradation. Hexavalent chromium (Cr(VI)) is not used in the tanning industry and has no effect in the tanning process (Rydin, 2002). The chromium(III)salts can, however – during certain conditions – be converted into Cr(VI) compounds. It is known that light and heat combined with the presence of oxidized fat can provoke the conversion of Cr(III) into Cr(VI) in certain leather types. It is furthermore known that the pH value significantly influences the state of which chromium will exist; hexavalent chromium (Cr(VI)) will reduce into trivalent chromium (Cr(III)) at low pH values.

1.1.1 Problems related to Cr(VI)

Studies have shown that leather products can release Cr(VI) compounds. Formerly, this was not believed possible since Cr(VI) under the influence of many organic compounds combined with a low pH value was expected to be reduced to Cr(III) compounds (Hauber and Germann, 1999). However, it is now known that leather products are able to release Cr(VI) compounds, which is a problem since hexavalent chromium compounds are contact allergens. Cr(VI) is regarded as one of the most well-known allergens. Contact allergy develops when reactive, low molecular weight substances such as chromium penetrate the skin and activate the immune system. This activation means that the immune system is able to recognise and react to the specific substance on re-exposure.

1.1.2 Problems related to Cr(III)

The majority of studies concerning allergy caused by chromium focus on Cr(VI). However, exposure to chromium through chromium-tanned leather can also include exposure to trivalent chromium (Cr(III)) compounds. The majority of Cr(III) compounds are bound to collagen-fibres in the leather, but it has been shown that a surplus of trivalent chromium compounds can be released from the leather during use. A study from 2006 (Hansen et al., 2006) examined the connection between foot-eczema and Cr(III) exposure. They found that patients with contact allergy to both Cr(III) and Cr(VI) had a larger risk of developing foot eczema than patients who only responded positively to Cr(VI). This indicated that Cr(III) plays a part in developing foot eczema. However, generally Cr(VI) is regarded as far more potent than Cr(III).

1.1.3 Cr(VI) can be avoided in the tanning process

Large chemical producing companies performed – in collaboration with the German leather institute "Reutlingen" – a thorough investigation of what causes the formation of Cr(VI) in leather products. They identified the critical steps in the production process. The critical steps were wet after-treatments, which includes neutralization, colouring, greasing, and after-tanning. They concluded that it was possible to avoid the problem with Cr(VI) in the leather. Information regarding how the substance can be avoided can be achieved by contacting suppliers of chemicals to the leather industry (TEGEWA, 1997) or by reading several international publications regarding leather (Hauber and Germann, 1999). In order to avoid Cr(VI) it is generally recommended to:

- avoid use of natural products such as fish oils
- employ vegetable retaining agents
- properly adjust pH values in neutralisation and
- avoid ammonia as a wetting agent before dyeing and instead use agents with reducing abilities. A higher moisture content during storage of the leather is positive for lowering or preventing Cr(VI).

Even though the most used method for tanning leather is based on the use of chromium, several other methods for tanning leather exist. Among these are:

- Vegetable-tanning which is a tanning process that uses tannin and other substances obtained from vegetable matter, tree bark, and other sources. The leather becomes supple and brown in colour with the exact shade depending on the mix of chemicals and the colour of the skin. However, vegetable-tanned leather is not stable in water and tends to discolour and when left to dry it will shrink and become less supple and harder.
- Aldehyde-tanning which is a tanning process that uses glutaraldehyde or oxazolidine. The leather becomes pale cream or white. The leather is often used in automobiles and shoes for infants. It is the main type of 'chromium-free' leather used.
- Synthetic-tanning, a process which uses aromatic polymers such as Novolac or Neradol types. The leather becomes white.

1.1.4 Magnitude of the potential problem

As described above both hexavalent chromium (Cr(VI)) as well as trivalent chromium (Cr(III)) can cause allergic reactions. Allergy caused by chromium is equally frequent amongst women and men. However, allergy caused by wearing leather shoes is particularly a problem amongst women which could be due to the fact that women more frequently than men wear sandals or stilettos with direct skin contact. Another reason could be the fact that women more often buy new shoes and that the exposure from migration of chromium may be higher in the first few months of wearing the shoe.

In a special edition of the German TV-station WDR's economy magazine "markt XL" on the subject "Children's Shoes: Poison in the Leather", the findings of a Cr(VI) pollution test performed on children's shoes are described as alarming. An overall number of 20 pairs of children's shoes from 16 different manufacturers were tested. Five of the 20 pair of shoes exceeded a threshold value of 3 mg/kg and hence they should not have been made commercially available in the first place. Another random test performed by

WDR in the previous year on the subject of "Summer Shoes: Risky Footwear" had already shown that almost a third of the shoes tested significantly exceeded the legal threshold value (CATS – The Cooperation for Avoiding Toxic substances in Shoes (date unknown, but after 2007)).

Recently, the Swedish Society for Nature Conservation (2009) has tested 21 pair of leather shoes from different parts of the world for the content of heavy metals and organic compounds. Most of the chemical compounds studied can be assumed to originate from the tanning, preservation or dyeing of the leather. Metals in various concentrations were found in all the shoes that were analysed. Extremely high levels of trivalent chromium were found in the shoes. The total amount of chromium was measured to be between 42 ppm and 29,000 ppm (which corresponds to 2.9%).

A study from the Danish EPA (Rydin, 2002) showed that chromium was released from 15 of 43 purchased leather products – equivalent to 35% of the purchased products. The leather products contained between 3.6 ppm and 14.7 ppm Cr(VI). The study also showed that some of the purchased baby shoes exceeded the limit for migration of chromium from toys according to the European Standard EN71.

1.1.5 Frequency of chromium allergy and causative exposures

In a recent study the development of chromium allergy among patients with eczema was investigated from 1985 to 2007 in the region of Copenhagen in Denmark. A retrospective analysis of contact allergy to chromium in 16,228 patients was made. The frequency of chromium allergy decreased significantly from 3.6% in 1985 to 1% in 1995, but increased again significantly to 3.3% in 2007. Cement exposures as cause of chromium allergy decreased after the regulation of Cr(VI) in cement while the frequency of relevant leather exposure increased significantly from 24.1% during 1989-1994 to 45.5% during 1995-2007. Most of these cases were caused by shoes. It was concluded that chromium allergy is currently increasing in Denmark due to leather exposure (Thyssen et al., 2009). Similar results have been reported from Germany (Geier et al., 2000).

Table 1-1: Causative exposures in chromium allergic patients (from Thyssen et al., 2009)

Causative exposures	Male patients (n=61) % (n)	Female patients (n=136) % (n)	Total (n=197) % (n)
Leather shoes	27.9 (17)	39.0 (53)	35.5 (70)
Leather gloves	23.0 (14)	5.1 (7)	10.7 (21)
Other leather goods	11.5 (7)	6.6 (9)	8.1 (16)
Cement	11.5 (7)	0	3.6 (7)
Plywood	3.3 (2)	0	1.0 (2)
Cosmetics	0	1.5 (2)	1.0 (2)
Graphic work and paint	4.9 (3)	0	1.5 (3)

The information described above clearly indicates that there is a potential problem with content (or more likely release) of chromium from leather products – especially shoes.

1.2 Purpose

The main purpose of this study is to clarify whether Cr(VI) and Cr(III) compounds are released from leather shoes sold in Denmark in an amount that constitutes a risk of causing allergic reactions.

To clarify this, the following activities have been performed:

- Market survey of amount of leather shoes available on the Danish market in 2008.
- Purchase of 60 pair of leather shoes from the Copenhagen area (20 lady's shoes, 20 men's shoes and 20 children's shoes).
- XRF (x-ray fluorescence) screening of the 60 leather shoes. Performed in order to get an indication of the amount of chromium present and thereby potentially create a selection criterion for choosing shoes to undergo further migration analysis.
- Migration analysis according to CEN EN ISO 17075: 2007 (an international accepted standard for determining Cr(VI) in solutions leached from leather) of 18 leather shoes.
- Health and risk assessment concerning allergy of the 18 leather shoes.

2 Relevant legislation

2.1 Regulation in Germany

Germany was the first country to introduce legislation regarding content of hexavalent chromium (Cr(VI)) in leather. In Germany the concentration of Chromium (VI) in leather products with longer skin contact (e.g. shoes, gloves, garment, leather used for toys and bags) is limited by the German "Bedarfsgegenständeverordnung" since August 2010. The concentration of Cr(VI) should be not detectable. The analytical method is given and the detection limit is 3 mg/kg. The analytical method given is very similar to ISO 17075.

No other countries have implemented legislation regarding content of hexavalent chromium in leather. However, several ecolabel schemes have defined limit values regarding content of hexavalent chromium in leather. The table below presents the limit values related to the different ecolabel schemes (quoted from Rydin, 2002).

Table 2-1: Limit values related to different ecolabel schemes.

Country	Organisation	Name	Year	Limit value – Cr(VI) mg/kg	Determination limit of analytical method
International	International Council of Tanners	Eco-Tox Label	1996	5	IUC 18 (3 mg/kg)
Germany	*	SG (Schadstoffgeprüft)	1997	Cannot be measured	DIN 53314 (3 mg/kg)
Germany	Lederinstitut Gerberschule Reutlingen	Test Mark for Leather	1997	Below determination limit (DIN 53314)	DIN 53314 (3 mg/kg)
EU	EU	Community Eco-Label for shoes (the EU flower)	1999	10	EN 420 (2 mg/kg)
International	TESTEX	Öko-Tex Standard 100	2000	Below determination limit (0.5 ppm)	Öko-Tex method** (0.5 ppm)
Catalonia	Department de Medi Ambienti	Distintiú de garantia de qualitat ambiental	2000	5	IUC 18 (3 mg/kg)
Brasil	Associaqao Brasileira de Normas Tecnicas	Marca ABNT-Qualidade Ambiental	1999	3	DIN 53314 (3 mg/kg)

* Prüf- und Forschungsinstitut Pirmasens: TÜV Rheinland Sicherheit und Umweltschutz GmbH; Institut Fresenius.
** Not publicly available.

2.2 Other regulatory initiatives

The liberation of hexavalent chromium (Cr(VI)) from chromated products has been tested with synthetic sweat. The liberation was compared to the results from the positive occlusive test gained from a clinical study of chromium-sensitized persons. Based on this, it was proposed that an industry standard level to minimize the risk of chromate allergy should be 0.3 $\mu g/cm^2$ (Wass and Wahlberg, 1991). An ECETOC task force recommended 5 ppm as an acceptable contamination level of nickel, cobalt, and chromium for consumer products, such as household products and cosmetics (Basketter et al., 1993). Later, this was reviewed and a limit below 1 ppm was recommended (Basketter et al., 2003).

In the regulation of Cr(VI) in cement the limit value is < 2 ppm in EU (directive) and in the U.S a very low limit of chromium as a wood preservative has been decided based on allergy as the critical health effect.

The information above indicates that the regulatory limits for Cr(VI) are fairly low and, in some cases, even below the level of determination according to ISO 17075. Furthermore, the information indicates that regulatory limits related to Cr(VI) have been based on allergy as the critical effect.

3 Market analysis and purchase

3.1 Market analysis of leather shoes in Denmark

The table below presents information related to the turnover of ladies' shoes, men's shoes, and other shoes in Denmark respectively - all shoes with leather components (for instance leather soles, leather strings, upper leather etc.). The numbers are from 2008 and retrieved from Statistics Denmark. It was not possible to retrieve data regarding specific sale of children's shoes. The category "other shoes" covers "unisex shoes" or simply "shoes".

Table 3-1: Import, export and turnover of leather shoes on the Danish market 2008.

	Industry – national sales	Import	Export	Turnover – Danish market 2008
Ladies' shoes	2,927,067 EUR	234,933,058 EUR	190,468,549 EUR	47,391,575 EUR
Men's' shoes	11,600 EUR	118,464,155 EUR	107,227,598 EUR	11,248,157 EUR
Other shoes	23,346,400 EUR	186,106,571 EUR	124,673,699 EUR	84,779,272 EUR
Total				143,419,004 EUR

Data source: www.dst.dk. Turnover is calculated as "Import – export" + "Industry national sales". The shoes all contain one or more leather components.(1 EUR = 7.5 DKK)

As seen in the table, the total turnover related to shoes with leather components in Denmark in 2008 is 143 mio. EUR. According to www.postdanmark.dk there are 2,649,337 households in Denmark (as of September 2009), which means that in 2008 each household spent in average 54 EUR on shoes with leather parts per year. With an average price of 74 EUR per pair of shoes (the average price of the shoes purchased in this project), this corresponds to an average purchase of 0.7 pair of leather shoes per household in 2008. Based on this information, it could be assumed that approximately 1.85 mio. pairs of leather shoes were sold on the Danish market in 2008. This only covers shoes with leather parts.

Hence, the market of shoes with leather components is relatively large in Denmark which supports the importance of evaluating whether there is a problem related to the content/release of chromium in leather shoes.

3.1.1 Major shoe chain stores

Based on a google-search and contact to the Danish Shoe Retailers Federation the following shoe chains/shops were identified in 2009 as the most well-known in Denmark:

Table 3-2: Well-known shoe chains/shops in Denmark

Well-known shoe chains/shops in Denmark
Bianco Footwear (franchise chain)
Banks Detail
ZJOOS (shopping-chain)
EuroSko (shopping-chain)
Feet me
Riis shoes
TOPS
Ecco
Skoringen (shopping-chain)

A request to the Danish Shoe Retailers Federation, which has 635 members (primarily shops but also suppliers), revealed the following market information regarding the shoe sector in Denmark. Of course, this information includes the sale of all types of shoes, not merely those including leather parts.

The present Danish shoe sector has approximately 630 shops organized in 6 capital chains, 5 buying groups, and individual shops. The 5 buying groups organize approximately 330 shops. The turnover in the Danish shoe sector is approximately 0.47 billion EUR. If shoes sold in e.g. sport shops and supermarkets are included, the total turnover amounts to approximately 0.67 – 0.73 billion EUR. More than 1200 shops sell shoes on the Danish market. The sale of shoes with leather parts comprises approximately 143 million EUR.

3.2 Purchase of 60 pairs of leather shoes

The market analysis resulted in the identification of the most well-known shoe chains in Denmark (see table above). Thus, the purchase strategy focused on making sure that shoes were bought from these shoe chains/stores. However, in order to make sure, that the purchased shoes represented the actual market of leather shoes in Denmark, shoes were also bought from other minor/lesser known shoe stores (including super markets, sport shops, etc.).

Only shoes with leather components that can come into contact with the skin were bought. Thus, shoes with for instance padding were not bought. The shopping focused on buying shoes that would be worn with bare feet (sandals, stilettos, etc.), or shoes which could be used during sports (perspiration) or shoes with a large surface area in contact with the skin (boots).

60 pair of shoes was bought within the Copenhagen area since it was judged that shoes bought within this area represented the type of shoes that are available on the Danish market. Shoes were bought in the following specific areas of Copenhagen:

- Inner city: Strøget, Købmagergade, Frederiksborggade, Østergade, Amagertorv, etc.
- Kgs. Nytorv: Magasin
- Lyngby: Lyngby Centre
- Amager: Field's

The purchases were completed in the period 30 September 2009 – 15 October 2009.

3.2.1 Distribution of purchased shoes according to type

Due to the purpose of the study (identifying potential health risks associated with skin contact to shoes), it was attempted to buy approximately 50% sandals (or similar) within each category (children's shoes, men's shoes, and lady's shoes), but due to the season (fall), it was not possible to reach that number, especially within the categories children's shoes and men's shoes. However, it was possible to buy a reasonable amount of boots within each category.

Table 3-3: Distribution of type of purchased shoes

	Children's shoes	Lady's shoes	Men's shoes
Shoes	13	3	16
Boots	4	7	3
Sandals	3	10	1
Total	*20*	*20*	*20*

3.2.2 Distribution of purchased shoes according to price

The purchased shoes represented a price-range between 10 EUR and 380 EUR per pair of shoe. The distribution of the purchased shoes according to price can be seen in the table below. The average price per pair of purchased shoe was 74 EUR.

Table 3-4: Distribution of purchased shoes according to price.

Price-range (EUR)	10-27	27-53	53-80	80-107	107-133	133-400	Total
Number of shoes	3	21	17	11	3	5	60

3.2.3 Distribution of purchased shoes according to country of origin

In approximately half of the purchases, it was possible to retrieve data regarding the country in which the shoe was manufactured. The results are presented in the table below.

Table 3-5: Distribution of shoes according to country of origin

Country of origin	Number of shoes
Belgium	1
Denmark	2
France	1
India	1
Italy	10
China	4
Mexico	1
Portugal	3
Spain	2
Germany	1
Asia	2
The shop did not know	32
Total	*60*

Out of the 28 shoes, of which it was possible to identify country of origin, 10 were from Italy. This indicates that the majority of the purchased shoes originate from Italy.

4 XRF screening of 60 leather shoes

The 60 pair of shoes was screened by use of an XRF instrument. Due to the fact, that the majority of the shoes had an inner-sole consisting of a different type of leather than the upper-leather, it was decided to screen each shoe at two different places – the sole (from inside the shoe) and the upper leather (from inside the shoe). In some cases, it was necessary to cut up the shoe in order to do a proper screening.

4.1 XRF screening – method and uncertainty

Results reached through a XRF screening indicate first and foremost which chemical elements that are present as well as their approximate proportional distribution with regard to amount. This semi-quantitative screening thus implies that there ***is*** a content of the chemical element in question; i.e. a positive quantitative determination. A strong signal implies that the leather part contains relatively large amounts of the element in question – weeks signal the opposite. Thus, the results do not represent a reliable value for the exact content of the chromium metal in percentages.

The level of detection is estimated to be 0.01%. Thus, samples that showed a content of chromium below this value (reported as <LOD) cannot be assumed with an absolute certainty not to contain chromium. Likewise it should be noted that only two types of leather samples (the inner sole and the upper leather on each shoe) were XRF screened on each shoe. Some of the shoes may contain several other leather pieces which were not analysed. Thus, it is unclear whether these parts included chromium. The risk of false-negative results is assumed to be insignificant, though at very low levels it cannot be excluded.

Finally, the results do not give any information about the state or form (ex. Cr(VI) or Cr(III)) of which the chemical element is present.

It is, however, judged that the results from the XRF screening are usable of selection of leather shoes for further migration analysis (for release of Cr(VI) and Cr(III) compounds).

4.2 Results from the XRF screening

4.2.1 Content of chromium according to shoe category (men's shoes, lady's, etc.)

The results from the XRF screening can be seen in Table 4-1 and Table 4-2. Table 4-1 presents the results from the XRF screening in the upper leather parts of the shoes, meaning the leather that surrounds the foot. 50 of the 60 purchased shoes had a content of chromium between 1 and 3% in the upper leather parts.

Table 4-2 shows the results from the XRF screening of the soles (from the inside of the shoes). In this case, 51 of the 60 purchased shoes had a content of chromium between 1 and 3%. Thus, it seems that the “typical” content of chromium in both soles and leather surrounding the foot is within the range of 1 to 3%. Though, as seen in Table 4-1 and Table 4-2 the majority of the shoes have a content of chromium in the range 1-2%. This corresponds to the recent findings of the Swedish Society for Nature Conservation (2009) where they examined the total chromium content of 21 pair of leather shoes from around the world. The majority of the shoes (19) had a total chromium concentration in the range between 1 and 3%.

It should be pointed out that it is to no surprise that almost all of the purchased shoes showed a content of chromium. This finding seems reasonable in view of the fact that the standard method of tanning leather is based on the use of chromium and in view of the fact that the XRF screening only indicates a content of the element chromium, it does not distinguish between Cr(III) and Cr(VI) compounds.

Three of the shoes did not seem to contain chromium (results listed as < LOD). Since the level of detection is 0.01% it cannot be ruled out that the shoes do contain a small amount of chromium. However, based on the limited amount of chromium found, it is likely that these shoes have been tanned without use of chromium sulphate, since it is, as described in section 1.1.3, possible to tan leather without use of chromium compounds.

The results of the XRF screening of all 60 shoes can be seen in appendix A.

The results show no indications of for instance men’s shoes having a higher content of chromium than lady’s shoes or children’s shoes.

Table 4-1: Content of chromium in upper leather parts

Chromium content (upper leather)	0	0-1%	1-2%	2-3%	3 - 3,3%	Total
Lady's shoes	0	4	9	7	0	20
Men's shoes	0	2	10	8	0	20
Children's shoes	0	2	8	8	2	20
Total	*0*	*8*	*27*	*23*	*2*	*60*

Table 4-2: Content of chromium in soles

Chromium content (sole)	0	0-1%	1-2%	2-3%	3 - 3,3%	Total
Lady's shoes	1	1	15	3	0	20
Men's shoes	0	0	13	6	1	20
Children's shoes	2	4	12	2	0	20
Total	*3*	*5*	*40*	*11*	*1*	*60*

4.2.2 Content of chromium according to shoe type (sandal, boots, etc.)

When comparing the chromium content of the upper leather from sandals, boots, and ordinary shoes, no correlation seems to be present. Thus, there is no indication that for instance boots are at a higher risk of containing large amounts of chromium than sandals.

Table 4-3: Content of chromium in upper leather in sandals, boots and ordinary shoes.

Chromium content (upper leather)	0	0-1%	1-2%	2-3%	3 - 3,3%	Total
Ordinary shoes	0	4	13	14	1	32
Sandals	0	4	8	2	0	14
Boots	0	0	6	7	1	14
Total no. of shoes	*0*	*8*	*27*	*23*	*2*	*60*

Table 4-4: Content of chromium in upper leather in sandals, boots and ordinary shoes in percentage.

Chromium content (upper leather)	0	0-1%	1-2%	2-3%	3 - 3,3%	Total
Ordinary shoes	0%	13%	44%	40%	3%	100%
Sandals	0%	29%	57%	14%	0%	100%
Boots	0%	0%	50%	43%	7%	100%

The data concerning chromium content in the inner-soles of the shoes is not presented here. However, the general picture is the same.

4.2.3 Content of chromium according to price of the shoe

As seen in the Table 4-5, the average chromium content within the different price-ranges seems to be somewhat similar (around 1.7 %) but with a slight increase in average chromium content in shoes within the higher price-range. As the amount of purchased shoes within the higher price-range is somewhat limited (5 pair of shoes), some uncertainties must be taken into consideration regarding determining this ‘trend’. Regarding the purchased shoes within the cheap price range (3 pair of shoes), the content of chromium is in average 0.9% - but also here some uncertainties must be taken into consideration regarding the ‘typical’ content of chromium due to the low number of purchased shoes in this price range.

Table 4-5: Content of chromium (in upper leather) according to price range.

Price-range (EUR)	10-27	27-53	53-80	80-107	107-133	133-400	Total
Number of shoes	3	21	17	11	3	5	*60*
Average content of chromium (%)	0.9	1.8	1.6	1.7	2.1	2.3	*1.8*

4.3 Summary of results

The XRF screening of the 60 shoes revealed that the typical range of chromium content in leather shoes seems to lie between 1 and 3%. Only 3 of the 60 shoes did not seem to contain chromium, i.e. the content was below the level of detection (0.01%).

Otherwise, the results indicated no correlation between content of chromium and shoe category (lady’s, men’s, or children’s shoes) or shoe type (sandals, boots or ordinary shoes).

However, the results demonstrated a slight increase in average chromium content in the more expensive shoes and a slight decrease in the chromium content in cheaper shoes. However, the number of shoes within these price-ranges is too low to verify this tendency.

Finally, the results showed that the chromium content in the upper leather often differs from the chromium content in the inner-sole. However, the typical range of chromium content is the same (between 1 and 3%). This seems reasonable in view of the fact that the type of upper leather often differs from the leather type used in the inner sole.

5 Migration analysis

5.1 Selection of shoes for migration analysis

Based on the results from the XRF screening shoes were selected to undergo migration analysis based on the following criteria:

- proportional equal distribution between shoe categories (lady's, men's and children's shoes)
- proportional equal distribution between shoe types (sandals, boots and ordinary shoes)
- proportional equal distribution between price range (though with a slight increase in the higher price range)
- proportional equal distribution of amount of chromium (however, the shoe having the highest amount of chromium content (3.3 %) was chosen as one of the shoes to undergo migration analysis).

Based on the criteria mentioned above, the shoes presented in Table 5-1, Table 5-2 and Table 5-3 were selected to undergo migration analysis. A total of 18 shoes were selected. The selection was based on the chromium content in the upper leather, since the upper leather typically constitutes the major part of "skin contact" and due to the fact that there seems to be a slight tendency to allergic reactions occurring on the upper foot (Nardelli et al., 2005). To further support the selection of shoes based on chromium content in the upper leather, it can be mentioned that the skin on the upper part of the foot is thinner than the skin underneath the foot, thus the risk of developing allergic reactions is probably higher on the upper part of the foot.

Table 5-1: Children's shoes selected for migration analysis.

Children's shoes	Price (EUR)	Product no.	Chromium (%) (upper leather)
Children's shoes - ordinary	73	15	1.5
Children's shoes - ordinary	57	36	3.3
Children's shoes - boot	93	53	1.3
Children's shoes - sandal	47	31	1.2
Children's shoes - sandal	37	61	*
Children's shoes - ordinary	8	60	0.3

**** the shoe was bought after XRF screening of the 60 shoes, thus no XRF result exist.***

Table 5-2: Lady's shoes selected for migration analysis.

Lady's shoes	Price (EUR)	Product no.	Chromium (%) (upper leather)
Lady's shoes - sandal	10	18	0.7
Lady's shoes - sandal	53	4	1.5
Lady's shoes - sandal	93	22	0.7
Lady's shoes - boot	149	37	2.3
Lady's shoes - boot	65	21	2.7
Lady's shoes - ordinary	380	44	2.4

Table 5-3: Men's shoes selected for migration analysis.

Men's shoes	Price (EUR)	Product no.	Chromium (%) (upper leather)
Men's shoes - ordinary	73	6	0.2
Men's shoes - sandal	33	63	*
Men's shoes - ordinary	80	24	1.5
Men's shoes - ordinary	80	28	1.7
Men's shoes - boot	93	62	*
Men's shoes - boot	53	48	1.6

***** *the shoe was bought after XRF screening of the 60 shoes, thus no XRF result exist.***

The 18 selected shoes represent shoes from Portugal, Italy, Mexico, France, and India as well as a number of shoes from "unknown sources". The majority of the selected shoes are bought in shoe stores. However, there are also examples of shoes from other types of shoe stores (clothing stores, malls, etc.). The shoes marked with a star (*) were bought after the XRF screening of the 60 shoes were completed. The reason for buying additional shoes (and performing migration analysis on these) was based on the fact that certain shoe types were lacking in the first shopping-spree (sport shoes and sandals for children and men). Thus, a second shopping-trip was performed in order to obtain these types of shoes.

5.2 Choice of analytical method

During the years, a number of test methods have been used to determine the content of hexavalent chromium (Cr(VI)) in products. However, some criticism has arisen related to how usable these test methods are. Therefore, prior to choosing a test method for this study, a minor survey related to the existing test methods was performed. During this survey, it became clear that the following two concerns have been discussed thoroughly among scientists dealing with measurements of Cr(VI):

Some argue that the high pH value in the extraction fluid (pH 7.5 – 8) used in the methods causes the formation of Cr(VI) compounds in the extraction fluid, which means that false-positive results arise.
Sweat has a lower pH value than the pH value used in the test methods. Cr(VI) can be reduced to Cr(III) in acid solutions, thus the extraction fluid would contain a higher concentration of Cr(VI) than would be found in sweat.

To clarify these concerns, Dr. Gerhard Nickolaus from Prüf- und Forschungsinstitut Pirmasens was contacted. Dr. Gerhard Nickolaus has worked with the challenges related to chromium in leather during the last 30 years and has been involved in the committees that developed the test methods. According to him:

1) Numerous tests have shown that Cr(VI) does not form in the extraction fluid used in the ISO 17075 method. He argues that, if Cr(VI) would be formed, then you would find Cr(VI) in all chromium-tanned leather which is not the case. Only in approximately 4-5% of the leather Cr(VI) is found.
2) In terms of the concerns related to the pH value in sweat, he mentions that there is no uniform sweat solution. Fresh perspiration, for instance, has a lower pH value than old perspiration which after microbial degradation can show alkaline reactions. Furthermore, he

mentions that shoes are often soaked with water (puddles, rain, etc.) – especially children's shoes. Therefore, after long discussions, the Committee decided that the best method was to extract Cr(VI) under conditions where Cr(VI) does not reduce to Cr(III) which would be the extraction solution and pH value used in the ISO 17075 method.

Based on this information, it was in this study chosen to analyse the shoes for Cr(VI) content based on the ISO 17075 method.

Hence, the upper leather of the 18 shoes selected in section 5.1 were analysed for migration of Cr(VI) and Cr(III) according to ISO 17075.

Below, the analysis methods are described in more details.

5.3 Description of method to determine Cr(VI) release

The International ISO Standard ISO 17075 specifies a method for determining Cr(VI) in solutions leached from leather under defined conditions.

Soluble Cr(VI) is leached (during a period of 3 hours) from the sample in phosphate buffer at pH 7.5 to 8.0 and substances which influence the detection are removed by solid phase extraction if necessary. The Cr(VI) in solution oxidizes 1,5-diphenylcarbazide to 1,5-diphenylcarbazone to give a red/violet complex with chromium, which can be quantified photometrical at 540 nm. The results obtained from the described method are strictly dependent on the extraction conditions. Results obtained by using other extraction procedures (extraction solution, pH, extraction time, etc.) cannot be compared with the results produced by the procedure described in this standard.

The method is suitable to quantify the Cr(VI) content in leathers in concentration of 3 mg/kg (3 ppm) or higher. This method is applicable to all leather types. More information can be found in the standard.

5.4 Description of method to determine Cr(III) release

The Cr(III) content will be determined by performing an analysis (by ICP-OES or similar) of the total chromium content in the extraction solution used for determining the Cr(VI) content - and then subtracting the value for the Cr(VI) content. This is possible due to the general accepted assumption that chromium is only present as elemental Cr(III) and Cr(VI).

The result is presented as mg Cr(III)/kg leather.

The result may be regarded as measurement of total potential skin exposure to chromium, Cr(VI) and Cr(III) from leather.

5.5 Results

The results from the ISO 17075 test of the 18 selected shoes can be seen in Table 5-4 below.

Table 5-4: Test results (ISO 17075) of Cr(VI) and Cr(III) leaching from the 18 leather shoes.

Shoe no.	Total Chromium mg/kg	Cr(VI) mg/kg	Cr(III) mg/kg	Type of shoe
4	*307*	***4,0***	*303*	***Lady's shoe - sandal***
6	*1*	<1	1	Men's shoe - ordinary
15	233	<1	233	Children's shoe – ordinary
18	*203*	***6***	*197*	***Lady's shoe - sandal***
21	*125*	***3***	*122*	***Lady's shoe - boot***
22	*246*	***4***	*242*	***Lady's shoe - sandal***
24	*98*	***62***	*36*	***Men's shoe - ordinary***
28	*42*	***6***	*36*	***Men's shoe - ordinary***
31	*156*	***33***	*123*	***Children's shoe - sandal***
36	218	<1	218	Children's shoe - ordinary
37	277	<1,5	276	Lady's shoe - boot
44	164	<1	163	Lady's shoe - ordinary
48	157	<1	157	Men's shoe - boot
53	147	<1	147	Children's shoe - boot
60	3	<1	3	Children's shoe - ordinary
61	159	<1	159	Children's shoe - sandal
62	<1	<1	<1	Men's shoe - boot
63	*73*	***16***	*57*	***Men's shoe - sandal***

Numbers highlighted represent shoes that exceed the determination level of 3 ppm Cr(VI).

8 of the 18 shoes analysed leached Cr(VI) in an amount equal to or above the determination limit of 3 ppm. The highest value detected was 62 ppm Cr(VI). Shoe no. 24 in table 5-4 representing this value was a white leather shoe (for men).

Of the 8 shoes leaching Cr(VI) 4 were lady's shoes, 3 were men's shoes, and 1 was a children's shoe.

Even though the determination level of the test method (ISO 17075) is 3 ppm, results below 3 ppm are presented as well (for instance < 1; 1, etc.). The reason for this being that the analytical method does reveal results below 3 ppm. However, these results are not fully reliable. A result of for instance 1 ppm indicates that the content is ***around*** 1, i.e. between perhaps 0.5 and 2. A result of <1 indicates that the content of chromium is likely to be below 1. Yet again, only results above 3 ppm can be assumed reliable.

6 Health assessment of chromium

In this report, the focus is on allergy caused by release of chromium from leather shoes.

6.1 Allergy to chromium

6.1.1 Contact allergy - mechanisms

Contact allergy develops when reactive, low molecular weight substances, such as chromium, penetrate the skin and activate the immune system. This activation means that the immune system is able to recognise and react to the specific substance on re-exposure. Contact allergy is also termed type IV-allergy and consists of two phases. A first phase, called the induction phase or sensitization, where the changes in the immune system are induced. This phase is without symptoms. On subsequent exposure to sufficient amounts of the allergenic substance, the immune system will react to the substance and symptoms will develop. This phase is called elicitation and the symptoms of elicitation are eczema, please see section 6.1.3.

6.1.2 Chromium as contact allergen

Chromium is a transitional metal that shows different oxidation states ranging from +2 to +6. However, only the trivalent Cr(III) and the hexavalent Cr(VI) oxidation states are sufficiently stable to act as contact allergens. In order to become allergenic, a low molecular weight substance must be able to bind to protein. As Cr(VI) does not react with protein. It is thought that Cr(VI) penetrates the skin and is reduced in the skin to Cr(III) to be able to act as an allergen.

6.1.3 Contact allergy to chromium – symptoms and consequences

The symptoms of contact allergy i.e elicitation are eczema which is itchy redness, papules, swelling, and some time blisters on the exposed skin area. In case of exposure to chromium released from leather shoes, foot eczema may develop (Figure 6-1).

Figure 6-1 Example of foot eczema.

The eczema can spread to other parts of the body if the exposure is continued. Once a person has developed allergy to chromium, it is a livelong condition where exposure to sufficient amounts of chromium will result in eczema. Exposure should be avoided. Otherwise the person may experience recurring or chronic eczema. Chromium allergy often gives rise to severe, chronic and therapy resistant eczema which may be due to the difficulties in avoiding exposures. Chromium-free shoes are recommended for persons who have developed chromium allergy to their shoes.

7 Exposure and risk assessment

Contact allergy consists of two phases, induction also called sensitization and elicitation as described above in section 6.1. Sensitization/induction is the phase where the substance induces specific changes in the immune system and is without symptoms. Elicitation is the following phase where a sensitized individual is re-exposed and develops symptoms (figure 6.1).

Exposure expressed as dose/cm^2 of an allergen is a decisive determinant for sensitization and elicitation (Friedmann et al., 1983; Robinson et al., 2000). Thus, the concentration of allergen released to or deposited on the skin from a given product is important. A dose-response relationship exists resulting in that the number of sensitized individuals will increase if the exposure dose increases and those sensitized will become more sensitive and react to lower doses upon re-exposure.

In addition to the concentration (i.e. dose) of allergen, other factors are of importance for development of allergy (sensitization and elicitation). In relation to shoes occlusion, moisture from sweat or weather conditions, micro-biological contamination, pH and pre-existing eczema of the feet will play a role for the risk of developing allergy to chromium. Further the number of exposures is important as the allergen will accumulate in the skin. In a recent experiment, the repeated low dose exposures were shown to induce sensitization to a similar degree as a single high dose exposure even though the total dose of all the low dose exposures was less than the high dose exposure (Paramasivan et al., 2010).

Exposure to the skin can be given in µg/cm^2 (over a given period of time) or converted to mg/kg (ppm) (over a given period of time).

7.1 Risk assessment methodologies and threshold values

7.1.1 Induction

In recent years, industry toxicologists have developed a risk assessment model for allergens in cosmetics. It is based on experimental induction data from human volunteers or animal experiments (www.ifraorg.org). It is based on the threshold doses (no effect or low effect doses) derived from the experiments, adjusted with safety factors and converted into different exposure scenarios e.g. for deodorants, lotions, lip products etc. (Gerberick 2001). The model has so far only been applied to fragrance ingredients in cosmetic products. There is no way to translate the model into assessing exposure from shoes as the conditions of exposure are very different in the two scenarios.

The Scientific Committee on Consumer Products (SCCP) advisory to the EU Commission made a critical evaluation of the risk assessment methodology in 2008 and concluded that it is a promising model but that the approach would mean increased exposure to allergens known to cause allergic contact dermatitis in consumers. Besides, the model aims exclusively at prevention of new cases of allergy and it does not take into account the existing allergy problem in the population. The Committee concluded that it had no confidence that the levels of skin sensitizers identified by the methodology are safe for the consumer (SCCP, 2008). This means that the model in its present form cannot be used to identify safe levels for neither sensitization nor elicitation.

7.1.2 Elicitation

An individual who has become sensitized to a substance will react to this particular substance upon re-exposure. Whether a sensitized individual will get symptoms depends on exposure, in particular concentration i.e. dose of allergen (see section 6.1). This concentration is different from person to person. However, when a group of individuals are studied dose-response curves can be drawn, which represent the group of sensitized individuals.

The curves are based on testing with a solution of the allergen in a small (0.5 cm^2) aluminium chamber under occlusion for two days on the back of the patient with allergy. The reaction is observed at each test site and the signs of allergic contact dermatitis are noted. This gives data on the threshold responses. Based on fitted dose-response curves, the dose, which will elicit a reaction in 10% of sensitized individuals, is estimated and often called $MET_{10\%}$ (minimal elicitation threshold) (Fischer et al. 2009). The results of such dose-response investigations employing allergic persons have been shown to be fairly reproducible even when these are performed in different clinics and in different European countries (Fischer et al. 2005, Hansen MB 2002). Even though no general model for the use of data yet has been accepted, such data has been the basis of several regulatory decisions regarding allergens.

7.1.3 Threshold values of chromium allergy from the literature

Existing data from humans usually takes precedence of results from animal studies in risk assessment. As described in the section above, a typical way of presenting threshold values related to allergenic effects is in terms of $MET_{10\%}$ values - which represent a value of which 10% of sensitized individuals elicit a reaction. The $MET_{10\%}$ is derived from one occluded exposure to a dose of allergen at 0.5 cm^2 area for 48 hours.

In similar exposure scenarios concerning chromium in cement and wood, concerning nickel in jewellery, and concerning dimethyl fumarate, a fungicide in shoes, elicitation data, such as $MET_{10\%}$ values, has been used directly in risk assessment. It is not possible to predict the exact induction level for a sensitizising substance based on knowledge of elicitation thresholds e.g. $MET_{10\%}$ values. But threshold values protecting sensitized individuals will be sufficiently low to protect against induction also (Basketter et al., 2001; SCCP 2008) and in this way target both primary and secondary prevention.

Threshold value for Cr(VI)

Data from several studies in humans exists concerning the elicitation thresholds for Cr(VI). The $MET_{10\%}$ from a single 48 hour occluded exposure has been estimated to be between 0.02-0.9 µg/cm^2 (see table 7-1) The most recent study is Danish and estimates the $MET_{10\%}$ to be 0.03 µg/cm^2, which corresponds to 1 ppm Cr(VI) over a period of 2 days (Hansen et al. 2003). This is in line with the results from the largest published study where the $MET_{10\%}$ was 3 ppm (Nethercott 1994). However, variations exist and both lower and more than 10 times higher $MET_{10\%}$ values have been identified (Hansen et al. 2002). The American EPA has based their risk assessment of allergy to chromium in wood on the study by Nethercott et al. (1994) as it was the largest study.

Table 7-1: Estimated Minimal Elicitation Threshold for 10% of sensitized individuals ($MET_{10\%}$).

$MET_{10\%}$ µg Cr(VI)/cm^2/2 days	Number of test subjects	Reference
0.09	54	Nethercott et al, 1994
0.35	14	Allenby & Goodwin, 1983
0.90	17	Kosann et al. 1998
0.02	5	Wass and Wahlberg, 1991
0.03*	18	Hansen MB et al 2003

* corresponded to 1 ppm (15µl of a solution with 1 mg/kg (ppm)=0.0001% CrVI applied at 0.5 cm^2 area of skin see Robinson et al, 2000)

Threshold value for Cr(III)

Only two studies concerning Cr(III) have been identified. The threshold levels identified for Cr(III) are higher than for Cr(VI). In the study by Nethercott et al. 1994, only 1 out of 54 patients reacted to Cr(III) corresponding to a threshold concentration of 33 µg/cm^2 (1099 ppm) while the estimated $MET_{10\%}$ for Cr(III) was 0.18 µg /cm^2 (6 ppm) in the study by Hansen et al. 2003 which is at least 6 times higher than for Cr(VI).

7.1.4 Examples of risk assessment of Cr(VI)

In four cases, risk assessments have been performed by regulatory authorities concerning chromium VI and contact allergy. These examples are described below.

South Korean toxicologists have assessed the safety of Cr(VI) in cosmetics by several models and concluded that 1 µg/cm^2 was safe for induction based on animal experiments (Local Lymph Node Assays) (Hwang et al 2009). Comment: The method used cannot be extrapolated to shoe exposure.

The American EPA chose the results of the study of Nethercott et al, 1994, mentioned in section 7.1.3, as the basis of limiting the risk of allergic reactions to Cr(VI) in treated wood. The threshold value of 0.09 µg/cm^2 (3 ppm) derived from the study was regarded the reference dose and a safety factor of 10 was applied so that the limit for Cr(VI) contents in wood became: 0.009 µg/cm^2 (0.3 ppm) The expert panel advising the EPA concluded that this dose should be protective against elicitation and would therefore also be protective against induction (US EPA, 2007).
Comment: The Nethercott et al. 1994 is the largest study performed concerning threshold values of Cr(VI). The exposure situation in wood is somewhat similar to shoes as exposure to wood may be due to bare feet walking or standing on wood floors. In both situations chromium has to be released from the product and deposited on the skin.

Since 1983 the contents of Cr(VI) in cement has been limited to <2ppm in order to protect construction workers from chromium allergy in Denmark. The limit was introduced in EU-legislation in 2005. No value is given concerning the dose/cm^2 and the basis of the original decision has not been recorded, but

it is believed to be based on practical considerations as well as potency and elicitation capacity of chromium, i.e. an expert judgment.
Comment: The limitation of Cr(VI) in cement to a level below 2 ppm has proven successful as the number of cases of chromium allergy due to cement exposure has been significantly reduced (Thyssen et al., 2009, Zachariae et al., 1996).

The German Risk assessment Institute (Bundesinstitut für Risikobewertung) issued the following statement (Federal Institut for Risk Assessment, 2007) in July 2007 recommending restrictions of Cr(VI) in leather goods: Studies by the regulatory authorities of the federal states reveal that many leather goods like gloves, shoes, or watch straps, which come into direct contact with the skin contain high levels of chromium (VI). Hexavalent chromium (Cr(VI)) is a strong allergen and it can lead to allergic skin reactions like contact eczema in sensitised individuals. The substance was detected in more than half the leather goods examined. In one sixth of the leather goods tested the levels were higher than 10 mg/kg leather (10 ppm). The only way of preventing allergic reactions is for allergy sufferers to avoid any contact with leather goods that contain chromium (VI). "More than half a million people in Germany react sensitively to this substance", says Professor Dr.. Andreas Hensel, President of the Federal Institute for Risk Assessment. "Therefore leather consumer goods, in particular leather clothing should not, in principle, contain any chromium (VI) at all". Hence BfR proposes restricting the use of chromium salts in leather production as far as possible or technically reducing their concentrations during processing to such an extent that chromium (VI) can no longer be detected in the end product".
Comment: This assessment, that low concentrations of Cr(VI), even below the determination level, may matter for chromium allergy, is in line with the American EPA and the regulation of Cr(VI) in cement.:

7.2 Risk assessment

7.2.1 Exposure measurements

The relevance of measurements of chromium release by DIN 53314, a method similar to ISO 17075, has previously been questioned in relation to the risk of eliciting chromium allergy (Hansen et al 2006). 15 subjects with Cr(VI) allergy were tested with different leather samples under occlusion at the back for 48 hours. The samples contained from <3 ppm to 16.9 ppm Cr(VI). No relationship between the measured contents of the Cr(VI) and Cr (III) of the leather and reactivity to the leather samples were seen after 48 hours. However, when the leather sample with the highest contents of Cr(VI) was worn for 14 days as a bracelet, it gave allergic reactions in 3 out of 12 people (25%). None had reacted to this sample when tested under 48 hour occlusion (Hansen et al 2006). This indicates that the exposure method is important and that the 48 hour occlusion test is not optimal to reveal leather samples which pose a risk of contact allergy, due to lack of sensitivity of the test. It may be that the leaching of chromium takes much longer time than 48 hours and special factors in the local environment e.g. pH and moisture unique for the shoe environment need to be present to promote the release of Cr(VI).

It is unknown how long time it will take chromium to leak from the shoes and become bio-available under standard and extreme use conditions. Further, other parameters may influence the direct skin exposure such as use of socks, their material, and personal hygiene habits. In the ISO 17075 the migration of chromium from 2 grams of leather is measured over a 3 hour period. The leather is cut into small pieces so the surface area is increased. The result may be regarded as measurement of total potential skin exposure to chromium, Cr(VI) and Cr(III) from leather.

Low levels of Cr(VI) may cause allergic contact dermatitis through a single occluded exposure. The lowest threshold levels, defined as $MET_{10\%}$, for a single occluded exposure to Cr(VI) which has been identified is in the range of 1 ppm to 3 ppm. Experiments show that even lower levels may elicit and induce sensitization to chemicals in general, if repeated exposures are performed (Paramasivan et al., 2010, Jensen et al., 2006).

The analytical method only gives reliable results above 3 ppm (3 mg/kg). Detectable Cr(VI) in leather shoes may therefore pose a risk of Cr(VI) allergy, and in fact, a non-quantifiable level of Cr(VI), i.e. below 3 ppm, does not indicate that there is no risk of Cr(VI) allergy, as the elicitation level of Cr(VI) is lower than the determination limit. Concerning Cr(III) few data exist regarding threshold values, which means that a definite risk assessment cannot be performed but the results may be used to define a potential area of concern.

7.2.2 Study results and risk of chromium allergy

In the current study 60 pair of shoes was screened for the content of total chromium by use of XRF instrument; 20 ladies shoes, 20 men's shoes, and 20 children's shoes. In 50 out of 60 shoes, a content of 1% to 3% chromium in the upper leather parts was found. This is not surprising as chromium is used for tanning of most leather products and the results correspond to another similar newer study. No correlation between shoe category (lady's shoes, men's shoes, children's shoes) or shoe type (boots, sandals, ordinary) and chromium contents was found but an indication of increasing chromium contents was found in expensive shoes, but definite conclusions cannot be reached as the number of samples were small in each category.

18 shoes were selected for migration analysis according to ISO 17085, six in each category and representing different types (sandals, shoes, and boots), different price ranges and equal distributions of chromium contents determined by the XRF screening. The analysis was performed on leather from the upper part of the shoes. It was found that 8 of the 18 analysed shoes had a Cr(VI) release higher than the determination limit of 3 mg/kg (3 ppm), median 6 ppm; range 3- 62 ppm. This is equal to 44% of the 18 shoes analysed according to ISO 17075. Furthermore, one shoe had a release of 1.5 ppm Cr(VI), but as this is below the determination limit, the result is not reliable.

All of these pair of shoes may pose a risk of causing Cr(VI) allergy in consumers. The reason being, that the analytical method only gives reliable results above 3 ppm (3 mg/kg) and the threshold limit for causing Cr(VI) allergy lies around 1 – 3 ppm, thus below the determinationlimit. Thus, shoes, which according to ISO 17075 does not seem to contain/release Cr(VI), may in fact still pose a risk of causing allergic reactions. At present time, no method exists, which can be used to determine with absolute certainty, that none of the leathershoes on the Danish market pose a risk of causing Cr(VI) allergy.

In general, the higher the dose of allergen the higher is the risk. The highest amount found was 63 ppm Cr(VI), found in a shoe for men, which will pose a considerable risk of Cr(VI) sensitization provided that the Cr(VI) is released under use conditions of the shoes. The same applies to the second highest value, which was 33 ppm, found in a sandal for children and the third, which was 16 ppm in a sandal for men. The remainder results were from 3 to 6 ppm Cr(IV), which is around the determination limit.

In total 3/8 (37.5%) of the shoes with a certain level of detectable Cr(VI) had a level higher than 10 ppm Cr(VI) or 3/18 (16.7%) of all the shoes, which underwent migration analysis. These results are similar to a German investigation performed by the German Risk Assessment Institute of more than 850 leather consumer items such as gloves and shoes (Brf, 2007). In the German investigation about half of the items released Cr(VI) above the analytical determination limit. In our investigation it was 44%, and in one sixth of the samples in the German investigation, the levels were higher than 10 ppm (mg/kg), similar to the findings in the current investigation.

Skin exposure to chromium released from leather is more intense if shoes are worn with bare feet and under humid conditions e.g. in summer time. Five of the shoes releasing Cr(VI) were sandals and this is 62.5% of those with a detectable Cr(VI) release. One was a boot and two were shoes. The reason for the content of Cr(VI) in the leather is unknown, as leather can be produced without leachable Cr(VI) without affecting the performance of the leather. However, it is quite unfortunate that the type of shoes which is most likely to be worn with bare feet and poses the highest direct exposure also were those releasing the highest amounts of Cr(VI), especially as one of them was a children's sandal.

Allergy to chromium from shoes is more frequent in women than men. In this investigation four of the eight shoes releasing Cr(VI) were ladies shoes, three were men's shoes and one children shoe. These findings do not explain the difference between women and men concerning risk of allergy. The higher risk of women of chromium allergy is thought to be due to women using sandals/stilettos and bare feet in shoes more often than men and possibly due to a higher turn over of shoes in women, which mean a higher accumulated risk (assuming that the amount of released Cr(VI) is higher in the beginning of the shoes 'lifetime').

In 10 pair of shoes, no detectable Cr(VI) was present which means that either very low levels or no Cr(VI) is present. It is not possible to exclude a risk of repeated exposures to even very small amounts of Cr(VI) can cause allergic reactions, as other elements related to, for instance, micro-biological contamination and different pH values (which affects the form of which chromium is present) will influence the risk of developing allergy. On the other hand, the risk increases with increasing doses.

Cr(III) migration was also quantified in the current investigation. The amount ranged from <0.5 mg/kg (ppm) to 303 ppm. Cr(III) may be converted into Cr(VI) and visa versa dependent on pH and other factors. Cr(III) binds easily to proteins and is therefore captured in the outer layers of the skin, the stratum corneum. Higher levels of Cr(III) than Cr(VI) are tolerated, as Cr(VI) is water soluble and easily penetrates skin. In one investigation, the threshold value $MET_{10\%}$ for Cr(III) was 0.18 µg/cm^2, corresponding to 6 ppm, which all the analysed shoes exceeded, except for two pairs. In another investigation, the corresponding threshold value was almost 200 times higher, that is above 1000 ppm Cr(III), which is above the content in all the shoes.

In the current investigation, no relation was seen between the release of Cr(VI) and the total content of Cr. Some of the shoes with high amounts of detectable Cr(VI) had low levels of total Cr e.g. shoes no. 63 and 24. Three shoes had no detectable Cr(VI) and very low levels of Cr(III) from <0.5 ppm to 3.3 ppm, which shows that it is possible to produce leather without significant amounts of leachable chromium and thus resulting in a low risk of allergy. It is estimated that 1.85 million pair of shoes with leather parts are sold in Denmark each year. In this investigation, 60 pairs were bought and 18 of these selected for migration analysis. All possible steps were taken to ensure that different types, categories and price levels were represented in the sample. Still, the 18 selected shoes is small sample in comparison with the total shoe market in Denmark. Even though there could be a bias in the selection it is unlikely to be systematic and the results are almost identical with those of a German investigation of more than 850 products, which supports the validity and the relevance of the findings to Danish consumers.

7.2.3 Conclusions

Detectable Cr(VI) in leather shoes may pose a risk of Cr(VI) allergy. In 8/18 of the shoes (44 %), in which the release of Cr(VI) was analysed, Cr(VI) was detected. In one sixth of the shoes, high levels of Cr(VI), defined as more than 10 ppm Cr(VI), were released. Sandals seemed to be over-represented among the shoes with detectable Cr(VI). This is of concern as sandals are more likely to be worn with bare feet and the direct exposure to Cr(VI) is likely to be higher. The shoe with one of the highest levels of Cr(VI) release was a children's sandal. No relation was found between Cr(VI) and Cr(III) levels. Due to limited (and to diverse) data regarding a threshold limit for the development of Cr(III) allergy, it was not possible to conclude anything regarding the risk of developing Cr(III) allergy by use of the shoes in this study.

The risk of using shoes that release chromium will be influenced by use conditions, such as moisture, pH, micro-biological contamination, and pre-existing skin diseases in a not yet determined way. It means that also shoes with releases a low level of Cr(VI) under certain conditions may pose a risk of chromium allergy. However, in general, the higher the dose of allergen the higher is the risk of allergy. Persons who already have developed Cr(VI) allergy may be so sensitive that they also react to levels of Cr(VI) below the determination level.

In three pair of shoes low levels of both Cr(VI) and Cr(III) were seen which indicates that it is technically possible to produce tanned leather without high levels of chromium and thus a reduced risk of chromium allergy.

Three pair of shoes did not show to contain chromium by XRF screening. However, the level of determination is 0.01%. Thus it cannot be ruled out that the shoes may contain a small amount of chromium. Yet, the levels are so low, that it can be assumed, that the leather is tanned by a method not applying chromium.

A Nickel directive was introduced in EU in 1994 and was based on a Danish regulation regarding the release of nickel from metal items in close contact with the skin. It has proven a very successful regulation, and a significant reduction in nickel allergy in young women has been found in Denmark following the regulation (Thyssen et al., 2009b). Based on this experience with nickel, a regulation of chromium in leather may be a way to reduce the number of chromium allergy cases.

All in all, the results of this study suggest, that there ***are*** problems related to a content and release of chromium from leather shoes on the Danish market. The full extend of the problem is, however, difficult to determine, since the determination limits of the available analytical methods, lie above the threshold value, that is assumed to cause allergic reactions toward Cr(VI).

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Appendix A – XRF test results of all 60 leather shoes

Test results of all 60 shoes (upper leather and inner sole). The level of detection (LOD) is estimated to 0.01%.

Shoe no.	Product type	Area tested	Chromium (%)
1	Lady's shoe - boot	inner sole	1,9
1	Lady's shoe - boot	upper leather	1,7
2	Lady's shoe - sandal	inner sole	2,1
2	Lady's shoe - sandal	upper leather	1,4
3	Lady's shoe - sandal	inner sole	1,9
3	Lady's shoe - sandal	upper leather	0,1
3	Lady's shoe - sandal	inner sole	0,1
4	Lady's shoe - sandal	upper leather	1,5
4	Lady's shoe - sandal	inner sole	1,4
5	Lady's shoe - boot	upper leather	2,1
5	Lady's shoe - boot	inner sole	1,0
6	Men's shoe - ordinary	inner sole	1,4
6	Men's shoe - ordinary	upper leather	0,2
7	Men's shoe - ordinary	upper leather	1,6
7	Men's shoe - ordinary	inner sole	1,6
8	Men's shoe - ordinary	upper leather	1,8
8	Men's shoe - ordinary	inner sole	1,6
9	Men's shoe - sandal	inner sole	1,7
9	Men's shoe - sandal	upper leather	0,7
10	Men's shoe - boot	inner sole	1,8
10	Men's shoe - boot	upper leather	1,6
11	Children's shoe - ordinary	upper leather	1,3
11	Children's shoe - ordinary	inner sole	0,7
12	Children's shoe - ordinary	inner sole	1,8
12	Children's shoe - ordinary	upper leather	1,7
13	Children's shoe - ordinary	upper leather	1,9
13	Children's shoe - ordinary	inner sole	0,8
14	Children's shoe - ordinary	upper leather	1,4
14	Children's shoe - ordinary	inner sole	0,9
15	Children's shoe - ordinary	upper leather	1,5
15	Children's shoe - ordinary	inner sole	1,4
16	Lady's shoe - sandal	upper leather	1,7
16	Lady's shoe - sandal	inner sole	1,3
17	Lady's shoe - ordinary	upper leather	2,0
17	Lady's shoe - ordinary	inner sole	1,8
18	Lady's shoe - sandal	upper leather	0,7
18	Lady's shoe - sandal	inner sole	< LOD

19	Lady's shoe - ordinary	upper leather	0,6
19	Lady's shoe - ordinary	inner sole	< LOD
20	Lady's shoe - sandal	upper leather	1,2
20	Lady's shoe - sandal	inner sole	1,2
21	Lady's shoe - boot	upper leather	2,7
21	Lady's shoe - boot	inner sole	2,0
22	Lady's shoe - sandal	inner sole	1,4
22	Lady's shoe - sandal	upper leather	0,7
23	Men's shoe - ordinary	inner sole	2,6
23	Men's shoe - ordinary	upper leather	2,6
24	Men's shoe - ordinary	upper leather	1,5
24	Men's shoe - ordinary	inner sole	1,2
25	Men's shoe - boot	upper leather	2,0
25	Men's shoe - boot	inner sole	1,9
26	Men's shoe - ordinary	inner sole	2,9
26	Men's shoe - ordinary	upper leather	2,6
27	Men's shoe - ordinary	upper leather	1,6
27	Men's shoe - ordinary	inner sole	1,4
28	Men's shoe - ordinary	inner sole	2,1
28	Men's shoe - ordinary	upper leather	1,7
29	Men's shoe - ordinary	upper leather	2,0
29	Men's shoe - ordinary	inner sole	2,0
30	Children's shoe - ordinary	upper leather	0,6
30	Children's shoe - ordinary	inner sole	< LOD
31	Children's shoe - sandal	inner sole	1,5
31	Children's shoe - sandal	upper leather	1,2
32	Children's shoe - ordinary	upper leather	2,4
32	Children's shoe - ordinary	inner sole	1,8
33	Children's shoe - boot	upper leather	2,3
33	Children's shoe - boot	inner sole	1,7
34	Children's shoe - ordinary	upper leather	2,1
34	Children's shoe - ordinary	inner sole	1,6
35	Children's shoe - boot	upper leather	3,2
35	Children's shoe - boot	inner sole	1,8
36	Children's shoe - ordinary	upper leather	3,3
36	Children's shoe - ordinary	inner sole	1,7
37	Lady's shoe - boot	upper leather	2,3
37	Lady's shoe - boot	inner sole	1,3
38	Lady's shoe - boot	upper leather	1,5
38	Lady's shoe - boot	inner sole	1,0
39	Lady's shoe - sandal	upper leather	2,2
39	Lady's shoe - sandal	inner sole	1,8
40	Lady's shoe - boot	upper leather	2,2
40	Lady's shoe - boot	inner sole	1,6
41	Lady's shoe - sandal	inner sole	2,1
41	Lady's shoe - sandal	upper leather	1,5
42	Lady's shoe - sandal	upper leather	1,7
42	Lady's shoe - sandal	inner sole	1,4
43	Lady's shoe - boot	inner sole	1,9
43	Lady's shoe - boot	upper leather	1,4
44	Lady's shoe - ordinary	upper leather	2,4
44	Lady's shoe - ordinary	inner sole	1,7
45	Men's shoe - ordinary	upper leather	2,0

45	Men’s shoe - ordinary	inner sole	1,1
46	Men’s shoe - ordinary	inner sole	3,0
46	Men’s shoe - ordinary	upper leather	2,4
47	Men’s shoe - ordinary	upper leather	2,0
47	Men’s shoe - ordinary	inner sole	1,8
48	Men’s shoe - boot	inner sole	1,7
48	Men’s shoe - boot	upper leather	1,6
49	Men’s shoe - ordinary	upper leather	1,6
49	Men’s shoe - ordinary	inner sole	1,2
50	Men’s shoe - ordinary	upper leather	1,7
50	Men’s shoe - ordinary	inner sole	1,7
51	Men’s shoe - ordinary	inner sole	2,7
51	Men’s shoe - ordinary	upper leather	1,7
52	Men’s shoe - ordinary	inner sole	2,6
52	Men’s shoe - ordinary	upper leather	2,5
53	Children’s shoe - boot	upper leather	1,3
53	Children’s shoe - boot	inner sole	0,9
54	Children’s shoe - ordinary	upper leather	2,0
54	Children’s shoe - ordinary	inner sole	1,1
55	Children’s shoe - sandal	upper leather	2,9
55	Children’s shoe - sandal	inner sole	2,4
56	Children’s shoe - ordinary	upper leather	2,6
56	Children’s shoe - ordinary	inner sole	1,0
57	Children’s shoe - ordinary	upper leather	2,6
57	Children’s shoe - ordinary	inner sole	1,6
58	Children’s shoe - sandal	inner sole	2,3
58	Children’s shoe - sandal	upper leather	1,7
59	Children’s shoe - boot	upper leather	2,6
59	Children’s shoe - boot	inner sole	1,1
60	Children’s shoe - ordinary	upper leather	0,3
60	Children’s shoe - ordinary	inner sole	0,0